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10/573,297	04/09/2007	Yusuke Nakamura	082368-007500US	6847

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EXAMINER

AEDER, SEAN E

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1642

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/573,297	Applicant(s) NAKAMURA ET AL.	
	Examiner SEAN E. AEDER	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20,23,25,28,98 and 99 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20,23,25,28,98 and 99 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Detailed Action

The Amendments and Remarks filed 5/7/08 in response to the Office Action of 2/7/08 are acknowledged and have been entered.

Claims 98-99 have been added by Applicant.

Claims 20, 23, 25, 28, 98, and 99 are pending.

Claims 20, 23, 25, and 28 have been amended by Applicant.

Claims 20, 23, 25, 28, 98, and 99 are currently under examination.

The following Office Action contains NEW GROUNDS of rejections.

Objections Withdrawn

The objection to the specification is withdrawn.

Rejection Withdrawn

The rejection under 35 U.S.C. 102(b) is withdrawn.

The rejection under 35 U.S.C. 102(e) is withdrawn.

New Objections

Specification

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Claims 20, 23, 25, 28, 98, and 99 recite inventions defined by Genbank accession numbers (see definition of BRC

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No. 456 located on page 83 of the specification). The sequences of the polypeptides used in the claimed invention are essential to practice the claimed invention, and the only disclosure of the sequences is made by references to published information outside of the specification. Therefore, information essential to practice the invention is incorporated by reference. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended claims 20, 23, 25, 28, 98, and 99 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying *candidate* compounds for treating or preventing cancer comprising contacting test compounds with T-LAK cell-originated protein kinase (encoded by BRC No. 456), detecting kinase activity of T-LAK cell-originated protein kinase, selecting test

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compounds that suppress the kinase activity of T-LAK cell-originated protein kinase as compared to the kinase activity of T-LAK cell-originated protein kinase detected in the absence of the test compounds, selecting test compounds that suppress cell growth as compared to cell growth detected in the absence of the test compounds, and selecting compounds that bind to T-LAK cell-originated protein kinase, wherein said selected compounds are candidate compounds for treating or preventing breast cancer, **the specification does not reasonably provide enablement for (1)** a method of screening for a compound for treating or preventing breast cancer comprising contacting a test compound with just any polypeptide encoded by just any polynucleotide of a gene of BRC No. 456, detecting binding activity between the polypeptide and the test compound, selecting the test compound that binds to the polypeptide, wherein every result is indicative of a compound that treats and prevents breast cancer or **(2)** a method for screening for a compound for treating or preventing cancer comprising contacting a test compound with just any polypeptide encoded by just any polynucleotide of a gene of BRC No. 456, detecting the kinase activity of said polypeptide, selecting a test compound that suppresses the kinase activity of said polypeptide as compared to the kinase activity of said polypeptide detected in the absence of the test compound, and further selecting test compounds that suppress cell growth as compared to cell growth detected in the absence of the test compound, wherein every test compound is useful for treating or preventing breast cancer. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The instant claims are broadly drawn to **(1)** a method of screening for a compound for treating or preventing breast cancer comprising contacting a test compound with just any polypeptide encoded by just any polynucleotide of a gene of BRC No. 456, detecting binding activity between the polypeptide and the test compound, selecting the test compound that binds to the polypeptide, wherein every result is indicative of a compound that treats and prevents breast cancer and **(2)** a method for screening for a compound for treating or preventing cancer comprising contacting a test compound with just any polypeptide encoded by just any polynucleotide of a gene of BRC No. 456, detecting the kinase activity of said polypeptide, selecting a test compound that suppresses the kinase activity of said polypeptide as compared to the kinase activity of said polypeptide detected in the absence of the test compound, and further selecting test compounds that suppress cell growth as compared to cell growth detected in the absence of the test compound,

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wherein every test compound is useful for treating or preventing breast cancer. This includes methods using just any polypeptide encoded by just any polynucleotide of a gene of BRC No. 456 to identify useful compounds for treating or preventing breast cancer. Further, this includes methods wherein every tested compound is useful for treating or preventing breast cancer. Further, this includes identifying compounds useful for treating and preventing breast cancer in vivo without obtaining any in vivo results.

This invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology". *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The specification teaches T-LAK cell-originated protein kinase mRNA is elevated in clinical breast cancer specimens as compared to corresponding normal breast controls (page 56, in particular). The specification further teaches siRNA specific for T-LAK cell-originated protein kinase inhibited proliferation of cultured breast cancer cells (page 57, in particular).

Further, the sequence of "BRC No. 456", defined as "Accession No. AF237709NM_018492", is critical or essential to the practice of the invention, but not included in the claim(s) and is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). In order to practice the invention, one of skill has to know the sequences of Accession No. AF237709NM_018492. Note the objection to the specification above. An amendment accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant,

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stating that the amendatory material consists of the same material incorporated by reference in the referencing application would obviate this part of rejection. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Further, therapeutic cancer treatments, in general, are unpredictable, as underscored by Gura (Science, 1997, 278:1041-1042.) who discusses the potential shortcoming of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated with cologenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041 first column, in particular) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive.

In regard to identifying compounds for preventing cancer, one of skill in the art would recognize that reasonable guidance with respect to preventing any cancer relies on quantitative analysis from defined populations which have been successfully pre-screened and are predisposed to particular types of cancer. This type of data might be derived from widespread genetic analysis, cancer clusters, or family histories. The essential element towards the validation of a preventive therapeutic is the ability to test the drug on subjects monitored in advance of clinical cancer and *link* those results with subsequent histological confirmation of the presence or absence of disease. This

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irrefutable link between antecedent drug and subsequent knowledge of the prevention of the disease is the essence of a valid preventive agent. Further, a preventive administration also must assume that the therapeutic will be safe and tolerable for anyone susceptible to the disease.

In regard to relying on in vitro assay or cell culture results to determine that a compound is useful for treating or preventing cancer, those of skill in the art recognize that in vitro assays and cell culture based assays are generally useful to observe basic physiological and cellular phenomenon such as screening *possible* effects of drugs. However, clinical correlations are generally lacking. The greatly increased complexity of the in vivo environment as compared to the very narrowly defined and controlled conditions of an in-vitro assay does not permit a single extrapolation of an in vitro assay to human efficacy with any reasonable degree of predictability. In vitro assays cannot easily assess cell-cell interactions that may be important in a particular pathological state. Furthermore, it is well known in the art that cultured cells, over a period of time, lose phenotypic characteristics associated with their normal counterpart cell type. Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, p4) teaches that it is recognized in the art that there are many differences between cultured cells and their counterparts in vivo. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation in vivo. Without this control,

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cellular metabolism may be more constant in vitro but may not be truly representative of the tissue from which the cells were derived. This has often led to tissue culture being regarded in a rather skeptical light (p.4, see Major Difference In Vitro). Further, Dermer (Bio/Technology, 1994, 12:320) teaches that, "Petri dish cancer" is a poor representation of malignancy, with characteristics profoundly different from the human disease. Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not. Yet normal or malignant cells in vivo are not like that. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years. Clearly it is well known in the art that cells in culture exhibit characteristics different from those in vivo and cannot duplicate the complex conditions of the in vivo environment involved in host-tumor and cell-cell interactions.

Further, those of ordinary skill in the art recognize that treatment in vivo is not predictive. The instant situation is analogous to that of *In re Brana* (34 U.S.P.Q. 2d 1436, 1440 (Fed. Cir. 1995)). A review of *In re Brana* reveals an application that claimed a chemical compound for treating a cancer, wherein the chemical compound was structurally similar to known compounds that have known in vivo use to treat tumors, and more importantly, Applicant provided in vivo data that the claimed compound could treat tumors in mice, hence it was ruled that the claimed compound was enabled for treating tumors. In the instant application, the claims are not drawn to

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methods which have been shown to predictably identify compounds which treat and prevent breast cancer in vivo. Further, the instant specification provides no in vivo data, particularly demonstrating that compounds identified by the claimed method would predictably give rise to a therapeutic effect in vivo. In view of *In re Brana*, Examiner asserts that successful use of in vivo mouse models of breast cancer enables compositions for specific therapeutic effects in humans and does not require human clinical testing; however, the instant application is claiming an in vitro method for identifying compounds that provide a therapeutic effect without providing any in vivo data, hence the claimed invention is not enabled. All of this underscores the criticality of providing workable examples which are not disclosed in the specification, particularly in an unpredictable art, such as cancer treatment and prevention.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to a method of screening for a compound for treating or preventing breast cancer comprising contacting a test compound with just any polypeptide encoded by just any polynucleotide of a gene of BRC No. 456, detecting binding activity between the polypeptide and the test compound, selecting the test compound that binds to the polypeptide, wherein every result is indicative of a compound that treats and prevents breast cancer, and Applicant has not enabled said method because it has not been shown that every compound contacted with just any polypeptide encoded by just any polynucleotide of a gene of BRC No. 456 is capable of treating and preventing breast cancer.

Further, one cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to a method for screening for a compound for treating or preventing cancer comprising contacting a test compound with just any polypeptide encoded by just any polynucleotide of a gene of BRC No. 456, detecting the kinase activity of said polypeptide, selecting a test compound that suppresses the kinase activity of said polypeptide as compared to the kinase activity of said polypeptide detected in the absence of the test compound, and further selecting test compounds that suppress cell growth as compared to cell growth detected in the absence of the test compound, wherein said test compound is useful for treating or preventing breast cancer, and Applicant has not enabled said method because it has not been shown that every compound contacted with just any polypeptide encoded by just any polynucleotide of a gene of BRC No. 456 is capable of treating and preventing breast cancer.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 20, 23, 25, 28, 98, and 99 are rejected under 35 U.S.C. 102(e) as being anticipated by Mack et al (US 2004/0005563; 1/8/04).

Claim 20 is drawn to a method comprising contacting a test compound with a polypeptide encoded by a polynucleotide of the gene of BRC No. 456, detecting the binding activity between the polypeptide and the test compound, and selecting the test compound that binds to the polypeptide. Claim 23 is drawn to a method comprising: (a) contacting a test compound with a polypeptide encoded by a polynucleotide of the gene of BRC No. 456; (b) detecting the kinase activity of the polypeptide of step (a); selecting the test compound that suppresses the kinase activity of the polypeptide encoded by the polynucleotide of the gene of BRC No. 456 as compared to the kinase activity of said polypeptide detected in the absence of the test compound; and (d) further selecting from the test compound selected in (c), the test compound that suppresses cell growth as compared to cell growth detected in the absence of the test compound, wherein said test compound is useful for treating or preventing cancer. Claim 25 is drawn to the method of claim 20, comprising the steps of: (a) contacting a test compound with a polypeptide encoded by a polynucleotide of the gene of BRC No. 456; (b) detecting the binding activity between the polypeptide and the test compound; and (c) selecting the test compound that binds to the polypeptide. Claim 28 is drawn to the method of claim 28 comprising: (a) contacting a test compound with a polypeptide encoded by a

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polynucleotide of the gene of BRC No. 456; (b) detecting the kinase activity of the polypeptide of step (a); and (c) selecting the test compound that suppresses the kinase activity of the polypeptide encoded by the polynucleotide of the gene of BRC No. 456 as compared to the kinase activity of said polypeptide detected in the absence of the test compound; and (d) further selecting, from the test compound selected in step (c), the test compound that suppresses cell growth as compared to cell growth detected in the absence of the test compound, wherein said test compound is useful for treating or preventing IDC. Claim 98 is drawn to the method of claim 20, further comprising the step of: (d) further selecting, from the test compound selected in step (c), the test compound that suppresses cell growth as compared to cell growth detected in the absence of the test compound. Claim 99 is drawn to the method of claim 25, further comprising the step of: (d) further selecting, from the test compound selected in step (c), the test compound that suppresses cell growth as compared to cell growth detected in the absence of the test compound.

It is noted that the “selecting” steps of claims 20, 23, 25, 28, 98, and 99 are not active steps and are not limitations to the claims. It is further noted that the “wherein” clauses of claims 23 and 28 are not active steps and are not required to be taught to anticipate the claims. It is further noted that the preambles of the instant claims are about intended purposes of the claimed methods are not considered limitations to the claims.

Mack et al refers to a polypeptide encoded by the polynucleotide of the gene of BRC No. 456 as “PDZ-binding kinase” (page 134, in particular). Mack et al further

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teaches expression of a polypeptide encoded by the polynucleotide of the gene of BRC No. 456 as "PDZ-binding kinase" is higher in ovarian cancer tissue as compared to a corresponding normal control (page 134, in particular). Mack et al further teaches a method comprising contacting a test compound with a polypeptide encoded by a polynucleotide of the gene of BRC No. 456, detecting the binding activity between the polypeptide and the test compound, selecting the test compound that binds to the polypeptide, and selecting a test compound that inhibits cell growth (paragraphs 51 and 92 and claim 23, in particular). Mack et al further teaches a method of determining whether a test compound inhibits kinase activity of a polypeptide encoded by the polynucleotide of the gene of BRC No. 456 as compared to the kinase activity of said polypeptide in the absence of said test compound (paragraph 206, paragraph 46, and claim 23, in particular).

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN E. AEDER whose telephone number is (571)272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean E Aeder/
Examiner, Art Unit 1642